

### **Remarks**

Claims 1-18 and 27-44 are pending in the application. Claims 1-14 and 27-40 have been amended.

Support for the amendments can be found throughout the application, including the claims as originally filed. Therefore, no new matter has been added. Importantly, the claim amendments should not be construed to be an acquiescence to any of the claim rejections. Rather, the amendments to the claims are being made solely to expedite the prosecution of the above-identified application. The Applicants expressly reserve the right to further prosecute the same or similar claims in subsequent patent applications claiming the benefit of priority to the instant application. 35 U.S.C. § 120.

### **Claim Rejections Based on 35 USC § 112¶2**

Claims 1-18 and 27-44 stand rejected under 35 U.S.C. § 112¶2 based on the Examiner's contention that they are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Applicants respectfully traverse this rejection. The Examiner's rejections are addressed below using the same headings as those in the Office Action.

a. Claims 1, 7, 11, 27, 33, 37.

The Examiner contends that claims 1, 7, 11, 27, 33, and 37 are indefinite because in the definition of  $R_{14}$ ,  $R$  in  $R_9C(O)OR$  and  $OC(O)R$  is not defined. The Applicants respectfully apologize for a typographical error in the rejected claims; the claims have been amended to correct the error. Specifically, claims 1, 7, 11, 27, 33, and 37 as amended include  $R_{16}C(O)OR_{15}$  and  $OC(O)R_{15}$  in the definition of  $R_{14}$ . The group  $R_{15}$ , heretofore  $R_8$ , is defined in each of these claims. Unfortunately, a unique subscript was mistakenly omitted from the Applicants' previous response when, in response to the Examiner's previous 35 U.S.C. § 112¶2 rejection, the term "ester" was replaced with structural formulas. The Applicants respectfully submit that every variable within the amended claims is properly and uniquely defined.

The Examiner contends that within claims 1, 7, 11, 27, 33, and 37 it is confusing to have two sets of definitions for R<sub>8</sub> and R<sub>9</sub> within the same claim: the R<sub>8</sub> and R<sub>9</sub> within the definitions of R<sub>2</sub>-R<sub>13</sub>; and the independent definitions for R<sub>8</sub> and R<sub>9</sub>. The Applicants respectfully apologize for this ambiguity due to an oversight. To remedy the ambiguity, the Applicants have amended the separate definitions of R<sub>8</sub> and R<sub>9</sub> to be R<sub>15</sub> and R<sub>16</sub>, respectively. Accordingly, R<sub>15</sub> “represents independently for each occurrence hydrogen, alkyl, alkenyl, alkynyl, or aryl”; and R<sub>16</sub> “represents independently for each occurrence a bond or an alkyl, alkenyl, alkynyl, or aryl biradical.” Also, the group that was previously defined as R<sub>15</sub> has been amended to be R<sub>17</sub>. The Applicants respectfully submit that the metes and bounds of every term used within the amended claim definitions would be clear to someone of ordinary skill in the art.

The Examiner contends that the definitions of R<sub>1</sub> and R<sub>2</sub>-R<sub>13</sub> in claims 1, 7, 11, 27, 33, and 37 are unclear because they contain the term “heteroaryl” which is not defined in the specification. The Examiner correctly points to page 8 of the specification where the terms “aryl heterocycles” and “heteroaromatics” are defined as aryls containing 1 to 4 heteroatoms. The Applicants have amended that paragraph in the specification to include the term “heteroaryl” as a coextensive term for referring to an aryl moiety containing 1 to 4 heteroatoms. The Applicants respectfully submit that this definition of heteroaryl is art-recognized and because the term appeared in the claims as originally filed, no new matter has been added.

b. Claims 3, 4, 9, 10, 13, 14, 29, 30, 35, and 36.

The Examiner contends that claims 3, 9, 13, 29, and 35 are indefinite because the term “alkoxy” has no antecedent basis; and claims 4, 10, 14, 30, and 36 are indefinite because the term “methoxy” has no antecedent basis. The Applicants respectfully traverse this rejection. Claims 3, 9, 13, 29, and 35 as amended do not include alkoxy, and claims 4, 10, 14, 30, and 36 as amended do not include methoxy. The Applicants respectfully submit that every term within the amended claim definitions has a proper antecedent basis.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 112¶2.

**Claim Rejections Based on 35 USC § 112¶1**

*Written Description*

Claims 1-18 and 27-44 stand rejected under 35 U.S.C. § 112¶1 based on the Examiner's contention that they fail to comply with the written description requirement. The Examiner contends that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner requests that the Applicants recite support in the specification for new terms R<sub>15</sub>, R<sub>16</sub>, Q<sub>1</sub> and Q<sub>2</sub>. The Applicants respectfully traverse this rejection.

The Applicants would like to remind the Examiner that these terms were introduced in the previous response to address a 35 U.S.C. § 112¶2 rejection made by the Examiner in an Office Action, issued September 9, 2002. In that office action, the Examiner referred to the various groups acyl, ether, sulfonyl, carbonyl, phosphoryl, amido, ester, etc. as "bivalent" even though it should be clear from formula I in claims 1, 7, 11, 27, 33, and 37 that the rules of valence require them to be monovalent groups bonded to the tropane framework.

Nevertheless, to remove any uncertainty the Examiner may have had, the Applicants replaced these art-recognized terms with structural formulas that explicitly show the point of attachment. Doing so required the introduction of terms R<sub>15</sub>, R<sub>16</sub>, Q<sub>1</sub> and Q<sub>2</sub>, but the Applicants want to stress that support for such terms comes from taking them together to define the various originally disclosed terms acyl, ether, sulfonyl, carbonyl, phosphoryl, amido, and ester, rather than considering them individually. If the Examiner maintains this written description rejection, then the Applicants respectfully submit that they should be able re-replace the structural formulas with the originally disclosed terms acyl, ether, sulfonyl, carbonyl, phosphoryl, amido, and ester because such terms are understood by one of ordinary skill in the art to be monovalent in the context of formula I.

### *Enablement*

Claims 1-4, 7-18, 27-30, and 33-44 stand rejected under 35 U.S.C. § 112¶1 based on the Examiner's contention that the Specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected to make and use the invention commensurate in scope with the claims. Specifically, the Examiner contends that 1) undue experimentation would be required for someone skilled in the art to make the compounds of the present invention, and that 2) there is no assurance that compounds of "such diverse" structures would be useful in inhibiting any monoamine transporters and thus be able to treat ailments associated with such activity. The Applicants respectfully traverse this rejection.

Regarding the Examiner's contention regarding making the compounds, the fourth paragraph on page 4 of the Examiner's Office Action states:

"In view of the high degree of unpredictability in the art, the limited examples and the scope of the claims does not commensurate with that of the objective enablement, one of ordinary skill in the art would not be able to make and use the invention as claimed without undue experimentation except for making and using the compound wherein R1 is aryl or heteroaryl, R2 to R13 being hydrogen, for inhibition of monoamine reuptake and for treating depression."

The Examiner appears to be taking the position that the Applicants are entitled only to the substituents actually prepared in the Exemplification section of the specification. This position is counter to federal appellate precedent interpreting the enablement requirement, even for an unpredictable art such as chemistry. *See, e.g., In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) ("As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied.")

The Applicants respectfully submit that the specification need only supply a reasonable correlation to the entire scope of the claims in light of the knowledge of one of ordinary skill in the art, and does not have to spell out how to prepare every species

within a claimed genus. Exhibits A-D were submitted by the Applicants in the previous Response to show the level of knowledge regarding tropanes attributable to one of ordinary skill in the art. The Examiner stated that the Applicants' Exhibits A-D, show two, or at most four substituents on the tropane ring and that this is quite different from the instant fourteen substituents presently claimed. The Applicants respectfully submit that the combined references show a total of fifteen substituents on the tropane ring, including H, ester, alkoxy, alkyl, alkenyl, alkynyl, ketone, formyl, aryl, aralkyl, amido, aryloxy, hydroxy, halide, and amino. Therefore, given the level of knowledge in tropane chemistry, the methods disclosed in the specification bear a reasonable correlation to the substituents presently claimed.

Regarding the Examiner's contention that there is no assurance that compounds of "such diverse" structures would be useful in inhibiting any monoamine transporters, the Applicants respectfully submit that the Examiner is impermissibly shifting a burden to the Applicants. See *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (CAFC 1995) ("The PTO has the initial burden of challenging a presumptively correct assertion of utility in the disclosure. Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's utility."). The Applicants respectfully submit that the Examiner has not satisfied her burden of providing evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility, especially in light of *In re Brana* which further states that although it is true that minor changes in chemical compounds can radically alter their effects on the human body, evidence of success in structurally similar compounds is relevant in determining whether one skilled in the art would believe an asserted utility. *Id.* at 1567.

Rather than offer any evidence that someone of ordinary skill in the art would doubt that the compounds of the claimed genus have monoamine transporter inhibiting properties, the Examiner has decided that the Applicants have exceeded an unstated ratio of claimed compounds to tested compounds, and have, therefore, failed to satisfy the

enablement requirement. Notwithstanding the fact that the compounds of the claimed genus share the same basic framework and differ only by the pendant R and A groups.

Consequently, the Applicants respectfully contend that armed with the exemplification provided in the instant application and the teachings in the scientific literature pertaining to tropane chemistry, one of ordinary skill in the art of synthetic organic chemistry would be able without undue experimentation to prepare compounds commensurate in scope with the claimed compounds, and would believe that they possess the requisite monoamine transporter inhibiting properties.

Accordingly, the Applicants respectfully request the withdrawal of the claim rejections based on 35 U.S.C. § 112¶1.

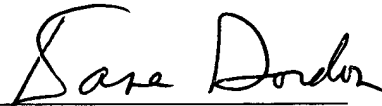
**Conclusion**

In view of the above amendments and remarks, the Applicants believe that the pending claims are in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite prosecution of the application, the Examiner is urged to contact the undersigned.

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